UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,324	12/10/2001	Francis J. Martin	55325-8148.US06	4133

22918 7590 12/30/2003

PERKINS COIE LLP
P.O. BOX 2168
MENLO PARK, CA 94026

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 12/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

COMMISSIONER FOR PATENTS
UNITED STATES PATENT AND TRADEMARK OFFICE
P.O. BOX 1450
ALEXANDRIA, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20031223

Application Number: 10/016,324
Filing Date: December 10, 2001
Appellant(s): MARTIN ET AL.

Jacqueline F. Mahoney
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10-03-03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences, which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

Claims 29-59 stand or fall together.

5,939,401	MARSHALL et al	8-1999
WO 86/06959	LIPOSOME TECHNOLOGY INC. (MIHALKO)	12-1986

5,800815	CHESTNUT et al.	9-1998
5,604,207	DeFREES et al	2-1997

Klibinov, A.L., et al. "Long-circulating liposomes: Development and Perspectives". J. Of Liposome Research, vol. 2, No. 3, (1992), pp. 321-324.

Gao, X., et al. "A Novel Cationic Liposome Reagent For Efficient Transfection Of Mammalian Cells" B.B.R.C., vol. 179, No. 1 (August 30, 1991), pp. 280-285.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

1. Claims 29-31, 33-37, 39 and 40-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Marshall (5,939,401).

Marshall discloses liposome formulations containing a cationic amphiphile, DOPE and PEG (5000)-DMPE for the administration of therapeutic molecules by inhalation. The biological molecules include proteins, small molecules, RNA and DNA. The cationic lipids include cholesterol carbamate derivatives (note the abstract, col. 34, line 27 et seq., col. 54, line 31 et. Seq.).

Appellant's arguments have been fully considered, but are not found to be persuasive. Appellant points out columns 15 and 33 of Marshall and argue that Marshall's structures are complexes and not liposomes. This argument is not found to be persuasive since Marshall's statements on col. 33, lines 33-49 pointed out by applicant himself, do not exclude the formation of liposomes also in his formulation. Marshall's statement only infers that structures other than highly organized vesicles are also effective. This statement does in no way infer that liposome structures are not present in Marshal and the claim language in instant claims does not exclude the

presence of other structures. Furthermore, the method of preparation as noted from Marshall's example 6 on col. 54 (lines 24-49) is a typical art known method of preparation of liposomes just as in instant method. Arguments that appellant's view is supported by Marshall's disclosure on col. 53, lines 46-53 (page 4 of the brief) regarding aggregation are not persuasive since no literature evidence is submitted to show that liposomes are stable particles with little tendency to aggregate. The statement therefore, is deemed to be speculative in nature. Similar is the case with appellant's statement with regard to no leakage of active agents from true liposomes (paragraph bridging pages 4 and 5 of the brief). Applicant argues that Marshall fails to teach a liposome having a coating of hydrophilic polymer chains on its surface. This argument is not found to be persuasive since Marshall's formulations contain PEG-DMPE; since as pointed out above, Marshall's formulations also include liposomal structures, it is implicit that the hydrophilic polymer structures extend outside the surface of the liposomes and therefore, the outer surface of the liposomes are coated. Instant claims do not require that the coating be continuous over the surface.

Appellant's arguments that Marshall's formulations do not have a biologically active agent are not found to be persuasive since Marshall on columns 33 and 34 describe the presence of biologically active agent.

Claim Rejections - 35 USC § 103

2. Claims 29-30, 34-37, 39-41, 44-49 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 86/06959 (Mihalko) in combination with Klibanov (J. Liposome Research, 1992) both are of record.

WO 86 (Mihalko) teaches liposomal formulations and a method of administering the formulations by inhalation. The liposomes are made from a variety of phospholipid combinations and having sizes of less than 5 microns. The encapsulated drugs include interferon (note the abstract, pages 8, 11, 12, 14, 19, 27, 28 and Examples). What is lacking in WO 86 is the teaching of the coating of the liposomal surface with a hydrophilic polymer.

Klibanov teaches that when the liposomal surface is coated with a hydrophilic layer of oligosaccharides, glycoproteins, polysaccharides and synthetic polymers such as PEG, the liposomes avoid the RES and circulate in blood for longer periods. Klibanov further teaches the targeting the liposomes using ligands such as biotin, proteins and antibodies (note the entire publication).

The coat the liposomes of WO 86 with a hydrophilic polymer would have been obvious to one of ordinary skill in the art because such a coating would enable the liposomes to circulate longer and reach the target tissue as taught by Klibanov.

Appellant's arguments have been fully considered, but are not found to be persuasive. Appellant argues that the purpose of the hydrophilic polymer is to shield the liposomes from RES whereas in Mihalko, the liposomes are administered by inhalation and therefore, there is no motivation to combine. This argument is not found to be persuasive since although the administration in Mihalko is by inhalation (just as in instant application), the purpose is to deliver the drug systemically and the inhaled drug in the liposomal formulation enters the blood for circulation. Therefore, it is reasonable

to expect the hydrophilic polymer to protect the liposomes in the blood from entering the RES and removed from circulation. Appellant's arguments with regard to the sizes of liposomes in Mihalko are not found to be persuasive since the statement on page 14, lines 14-15 of the reference indicates the less crucial nature of the liposomal sizes. Furthermore, instant claims do not recite any size limitations.

3. Claims 29-31, 33-37, 39 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marshall cited above by itself or in combination with WO 86/06959 cited above.

As pointed out above, Marshall discloses liposome formulations containing a cationic amphiphile, DOPE and PEG (5000)-DMPE for the administration of therapeutic molecules by inhalation. The biological molecules include proteins, small molecules, RNA and DNA. The cationic lipids include cholesterol carbamate derivatives (note the abstract, col. 34, line 27 et seq., col. 54, line 31 et. Seq.). Marshall does not provide a specific example showing the administration by inhalation. It would have been obvious to one of ordinary skill in the art to use this mode of administration of liposomes suggested by Marshall since the mode of administration is the choice of the practitioner. One of ordinary skill in the art would be motivated to use the inhalation route since WO shows that this route as a successful mode of administration of liposomes.

Appellant's arguments have been fully considered, but are not found to be persuasive. Appellant's arguments with regard to Marshall have been addressed above. Applicant once again argues about the sizes of the liposomes in Mihalko. These arguments are not found to be persuasive since as pointed out above, the statement of Mihalko on page 14 indicate the less crucial nature of the liposomal sizes and instant claims do not recite any size limitations.

4. Claims 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marshall cited above by itself or in combination with WO 86/06959 cited above, further in view of Gao (BBRC, 1991).

The teachings of Marshall have been discussed above. Marshall teaches cholesterol derivatives, but not instantly claimed dimethylaminoethane carbamoyl cholesterol.

Gao teaches that instant carbamoyl cholesterol in liposomes is very effective transfecting agent (note the abstract). It would have been obvious to one of ordinary skill in the art to use instant carbamoyl cholesterol derivative in Marshall's liposomes since Gao teaches that this cationic lipid is an effective transfection agent.

Appellant's arguments that the teachings of Gao and Huang do not make up the deficiencies since they make no mention of hydrophilic polymer chains or of coating a liposome with hydrophilic chains are not found to be persuasive since these references have been combined for the teachings of carbamoyl cholesterol derivative since this cationic lipid is an effective transfection agent.

5. Claims 49-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 86/06959 in combination with Klibanov (J. Liposome Research, 1992), further in view of Chestnut (5,800,815), DeFrees (5,604,207) and applicant's statements of prior art.

The teachings of WO and Klibanov have been discussed above. Neither WO nor Klibanov teach instantly claimed antibodies and ligands.

Chestnut teaches targeting of liposomes using selectin antibodies (note col. 21).

DeFrees teaches targeting of liposomes using sialyl LE (note columns 47 and 48). Applicants indicate that the claimed antibodies and other ligands are art known (see Table I on page 23).

It would have been obvious to one of ordinary skill in the art to use art known ligands in the teachings of WO and Klibanov since Klibanov teaches that targeting ligands such as proteins and antibodies can be attached to the liposomal surface and the references of Chestnut and DeFrees further provide guidance as to use of the ligands such as selectin antibodies and sialyl Le along with liposomes.

Appellant's arguments that the teachings of Chestnut, and DeFrees do not make up the deficiencies since they make no mention of hydrophilic polymer chains or of coating a liposome with hydrophilic chains are not found to be persuasive since these references have been combined for the teachings of targeting ligands.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/S Kishore/

Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK
December 23, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Conferees

/Edward J. Webman/

EDWARD J. WEBMAN
PRIMARY EXAMINER
GROUP 1500

PERKINS COIE LLP
P.O. BOX 2168
MENLO PARK, CA 94026